

Secret Paper 8

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NEWS 25 Dec 10 WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 26 Dec 10 DGENE BLAST Homology Search

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=> s zinc finger
L1 12117 ZINC FINGER

=> s l1 and (two or 2) (2A) (domain)
L2 590 L1 AND (TWO OR 2) (2A) (DOMAIN)

=> s l1 and ((two or 2) (2A) (domain or regulat? or inhibit?))
L3 803 L1 AND ((TWO OR 2) (2A) (DOMAIN OR REGULAT? OR INHIBIT?))

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L4 225 L1 AND ((TWO OR 2) (2A) (REGULAT? OR INHIBIT?))

=> s l4 and py<1999
L5 133 L4 AND PY<1999

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ENTER L# LIST OR (END):5
5 IS NOT VALID HERE
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L6 82 DUPLICATE REMOVE L5 DUPLICATE REMOVE L5 (51 DUPLICATES REMOVED)

=> d 1-10 bib ab

L6	ANSWER 1 OF 82	MEDLINE	DUPLICATE 1
<u>Full-text</u>			
AN	1998434612	MEDLINE	
DN	98434612	PubMed ID: 9756940	
TI	The early growth response protein (EGR-1) regulates interleukin-2 transcription by synergistic interaction with the nuclear factor of activated T cells.		
AU	Decker E L; Skerka C; Zipfel P F		
CS	Research Group of Biomolecular Medicine, Bernhard Nocht Institute for Tropical Medicine, Bernhard-Nocht-Strasse 74, D-20359 Hamburg, Germany.		
SO	JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 9) 273 (41) 26923-30.		

Journal code: HIV; 2985121R. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199811

ED Entered STN: 19990106

Last Updated on STN: 19990106

Entered Medline: 19981102

AB The early growth response-1 gene (EGR-1) is induced by a wide range of stimuli in diverse cell types; however, EGR-1-regulated genes display a highly restricted pattern of expression. Recently, an overlapping Sp1.EGR-1 binding site has been identified within the interleukin-2 (IL-2) gene promoter directly upstream of the binding site for the nuclear factor of activated T cells (NFAT). We used transfection assays to study how the abundantly and constitutively expressed Sp1 protein and the immediate early EGR-1 **zinc finger** protein **regulate** IL-2 gene expression. Here, we identify EGR-1 as an important activator of the IL-2 gene. In Jurkat T cells, EGR-1 but not Sp1 acts as a potent coactivator for IL-2 transcription, and in combination with NFATc, EGR-1 increases transcription of an IL-2 reporter construct 200-fold. Electrophoretic mobility shift assays reveal that recombinant EGR-1 and NFATc bind independently to their target sites within the IL-2 promoter, and the presence of both sites on the same DNA molecule is required for EGR-1.NFATc.DNA complex formation. The transcriptional synergy observed here for EGR-1 and NFATc explains how the abundant nuclear factor EGR-1 contributes to the expression of restrictively expressed genes.

L6 ANSWER 2 OF 82

MEDLINE

DUPLICATE 2

Full-text

AN 1998250719 MEDLINE

DN 98250719 PubMed ID: 9582305

TI Nonmyogenic factors bind nicotinic acetylcholine receptor promoter elements required for response to denervation.

AU Bessereau J L; Laudenbach V; Le Poupon C; Changeux J P

CS Neurobiologie Molculaire, UA CNRS D1284, Departement des Biotechnologies, Institut Pasteur 25/28 rue du Dr. Roux, 75724 Paris Cedex 15, France.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 May 22) 273 (21) 12786-93.

Journal code: HIV; 2985121R. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199806

ED Entered STN: 19980708

Last Updated on STN: 19980708

Entered Medline: 19980625

AB Nicotinic acetylcholine receptors (AChRs) belong to a class of muscle proteins whose expression is regulated by muscle electrical activity. In innervated muscle fiber, AChR genes are transcriptionally repressed outside of the synapse, while after denervation they become reexpressed throughout the fiber. The myogenic determination factors (MDFs) of the MyoD family have been shown to play a central role in this innervation-dependent regulation. In the chicken AChR alpha-subunit gene promoter, two E-boxes that bind MDFs are necessary to achieve the enhancement of transcription following muscle denervation. However, the deletion of promoter sequences located upstream to these E-boxes greatly impairs the response to denervation (Bessereau, J. L., Stratford-Perricaudet, L. D., Piette, J., Le Poupon, C. and Changeux, J. P. (1994) Proc. Natl. Acad. Sci. U. S. A. 91, 1304-1308). Here we identified **two**

additional **cis-regulatory** elements of the alpha-subunit gene promoter that cooperate with the E-boxes in the denervation response. One region binds the Spl and Sp3 **zinc finger** transcription factors. The second region binds at least three distinct factors, among which we identified an upstream stimulatory factor, a b-ZIP-HLH transcription factor. We propose that among MDF-responsive muscle promoters, a specific combination between myogenic and nonmyogenic factors specify innervation-dependent versus innervation-independent promoters.

L6 ANSWER 3 OF 82 MEDLINE

DUPLICATE 3

Full-text

AN 1998216760 MEDLINE

DN 98216760 PubMed ID: 9557682

TI Cloning of novel isoforms of the human Gli2 oncogene and their activities to enhance tax-dependent transcription of the human T-cell leukemia virus type 1 genome.

AU Tanimura A; Dan S; Yoshida M

CS Department of Cellular and Molecular Biology, Institute of Medical Science, University of Tokyo, Japan.

SO JOURNAL OF VIROLOGY, (1998 May) 72 (5) 3958-64.
Journal code: KCV; 0113724. ISSN: 0022-538X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

OS GENBANK-AB007295; GENBANK-AB007296; GENBANK-AB007297; GENBANK-AB007298

EM 199805

ED Entered STN: 19980529

Last Updated on STN: 19980529

Entered Medline: 19980520

AB The expression of human T-cell leukemia virus type 1 (HTLV-1) is activated by interaction of a viral transactivator protein, Tax, and cellular transcription factor, CREB (cyclic AMP response element binding protein), which bind to a 21-bp enhancer in the long terminal repeats (LTR). THP (Tax-helping protein) was previously determined to enhance the transactivation by Tax protein. Here we report novel forms of the human homolog of a member of the Gli oncogene family, Gli2 (also termed Gli2/THP), an extended form of a **zinc finger** protein, THP, which was described previously. Four possible isoforms (hGli2 alpha, beta, gamma, and delta) are formed by combinations of two independent alternative splicings, and all the isoforms could bind to a DNA motif, TRE2S, in the LTR. The longer isoforms, alpha and beta, were abundantly expressed in various cell lines including HTLV-1-infected T-cell lines. Fusion proteins of the hGli2 isoforms with the DNA-binding domain of Gal4 activated transcription when the reporter contained a Gal4-binding site and one copy of the 21-bp sequence, to which CREB binds. This activation was observed only in the presence of Tax. The 21-bp sequence in the reporter was also essential for the activation. These results suggest that simultaneous binding of hGli2 and CREB to the respective sites in the reporter seems to be critical for Tax protein to activate transcription. Consequently, it is probable that the LTR can be **regulated** by **two** independent signals through hGli2 and CREB, since the LTR contains the 21-bp and TRE2S sequences in the vicinity.

L6 ANSWER 4 OF 82 BIOSIS COPYRIGHT 2001 BIOSIS

Full-text

AN 1998:296836 BIOSIS

DN PREV199800296836

TI XRCC1 is specifically associated with poly(ADP-ribose) polymerase and negatively regulates its activity following DNA damage.

AU Masson, Murielle; Niedergang, Claude; Schreiber, Valerie; Muller, Sylviane; Menissier-De Murcia, Josiane; De Murcia, Gilbert (1)
 CS (1) Ecole Superieure Biotechnol. Strasbourg, UPR 9003 Cent. Natl. Rech. Sci., Boulevard S. Brant, F-67400 Illkirch-Graffenstaden France
 SO Molecular and Cellular Biology, (June, 1998) Vol. 18, No. 6, pp. 3563-3571.
 ISSN: 0270-7306.
 DT Article
 LA English
 AB Poly(ADP-ribose) polymerase (PARP; EC 2.4.2.30) is a **zinc-finger** DNA-binding protein that detects and signals DNA strand breaks generated directly or indirectly by genotoxic agents. In response to these breaks, the immediate poly(ADP-ribosyl)ation of nuclear proteins involved in chromatin architecture and DNA metabolism converts DNA damage into intracellular signals that can activate DNA repair programs or cell death options. To have greater insight into the physiological function of this enzyme, we have used the two-hybrid system to find genes encoding proteins putatively interacting with PARP. We have identified a physical association between PARP and the base excision repair (BER) protein XRCC1 (X-ray repair cross-complementing 1) in the *Saccharomyces cerevisiae* system, which was further confirmed to exist in mammalian cells. XRCC1 interacts with PARP by its central region (amino acids 301 to 402), which contains a BRCT (BRCA1 C terminus) module, a widespread motif in DNA repair and DNA damage-responsive cell cycle checkpoint proteins. Overexpression of XRCC1 in Cos-7 or HeLa cells dramatically decreases PAR-P activity in vivo, reinforcing the potential protective function of PARP at DNA breaks. Given that XRCC1 is also associated with DNA ligase III via a second BRCT module and with DNA polymerase beta, our results provide strong evidence that PARP is a member of a BER multiprotein complex involved in the detection of DNA interruptions and possibly in the recruitment of XRCC1 and its partners for efficient processing of these breaks in a coordinated manner. The modular organizations of these interactors, associated with small conserved domains, may contribute to increasing the efficiency of the overall pathway.

L6 ANSWER 5 OF 82 MEDLINE DUPLICATE 4

Full-text

AN 1998188225 MEDLINE
 DN 98188225 PubMed ID: 9520388
 TI Myeloid-specific transcriptional activation by murine myeloid **zinc-finger** protein 2.
 AU Murai K; Murakami H; Nagata S
 CS Osaka Bioscience Institute, 6-2-4 Furuedai, Suita, Osaka 565, Japan.
 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Mar 31) 95 (7) 3461-6.
 Journal code: PV3; 7505876. ISSN: 0027-8424.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199805
 ED Entered STN: 19980514
 Last Updated on STN: 19980514
 Entered Medline: 19980501
 AB Myeloid **zinc finger** protein 2 (MZP-2) is a **zinc-finger** transcription factor that is expressed in myeloid cells, particularly in the cells committed to the neutrophilic lineage. Here we examine the ability of murine MZF-2 (mMZP-2) to activate transcription. The mMZP-2 protein binds to a DNA element (MZP-binding site) through its **zinc-finger** domain. When the intact mMZP-2 was cotransfected with a

reporter gene, it did not activate transcription. However, N-terminal deletion mutants greatly enhanced transcription specifically in myeloid cells. Furthermore, in an in vivo competition assay, the middle region of MZF-2 **inhibited** the mMZF-2-mediated transcription activation. These results suggest that mMZF-2 is a transcriptional factor that can specifically work in myeloid cells and can be divided into at least three functional domains. The N-terminal domain inhibits transactivation by masking the effect of the activation domain. The middle region recruits a coactivator, which is responsible for myeloid-specific transcriptional activation. The C-terminal **zinc-finger** domain functions as a DNA-binding domain.

L6 ANSWER 6 OF 82 MEDLINE

DUPLICATE 5

Full-text

AN 1998113171 MEDLINE

DN 98113171 PubMed ID: 9442049

TI Divergent transcriptional control of multidrug resistance genes in *Saccharomyces cerevisiae*.

AU Hallstrom T C; Moye-Rowley W S

CS Molecular Biology Program, University of Iowa, Iowa City 52242, USA.

NC GM49825 (NIGMS)

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Jan 23) 273 (4) 2098-104.

Journal code: HIV; 2985121R. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199803

ED Entered STN: 19980312

Last Updated on STN: 19980312

Entered Medline: 19980303

AB Improper control of expression of ATP binding cassette transporter-encoding genes is an important contributor to acquisition of multidrug resistance in human tumor cells. In this study, we have analyzed the function of the promoter region of the *Saccharomyces cerevisiae* YOR1 gene, which encodes an ATP binding cassette transporter protein that is required for multidrug tolerance in *S. cerevisiae*. Deletion analysis of a YOR1-lacZ fusion gene defines three important transcriptional **regulatory** elements. **Two** of these elements serve to positively regulate expression of YOR1, and the third element is a negative regulatory site. One positive element corresponds to a Pdr1p/Pdr3p response element, a site required for transcriptional control by the homologous **zinc finger** transcription factors Pdr1p and Pdr3p in other promoters. The second positive element is located between nucleotides -535 and -299 and is referred to as UASYOR1 (where UAS is upstream activation sequence). Interestingly, function of UASYOR1 is inhibited by the downstream negative regulatory site. Promoter fusions constructed between UASYOR1 and the PDR5 promoter, another gene under Pdr1p/Pdr3p control, are active, whereas analogous promoter fusions constructed with the CYC1 promoter are not. This suggests the possibility that UASYOR1 has promoter-specific sequence requirements that are satisfied by another Pdr1p/Pdr3p-regulated gene but not by a heterologous promoter.

L6 ANSWER 7 OF 82 MEDLINE

DUPLICATE 6

Full-text

AN 1999010933 MEDLINE

DN 99010933 PubMed ID: 9796909

TI **Inhibition** of IL-2 production by Nil-2-a in murine T cells.

AU Pucci S; Doria G; Barile S; Pioli C; Frasca D

CS Laboratory of Immunology, AMB-PRO-TOSS, ENEA CR Casaccia, St Maria di

Galeria (Rome), Italy.

SO INTERNATIONAL IMMUNOLOGY, (1998 Oct) 10 (10) 1435-40.
Journal code: AY5; 8916182. ISSN: 0953-8178.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199902

ED Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990203

AB The loss of IL-2 production is the main defect accounting for age-related immunodeficiencies. We have investigated the molecular mechanisms involved in the decrease of IL-2 production in CD4+ T cells from aging mice. Our results demonstrate that the stability of IL-2 mRNA increases in T cells from young mice, whereas it declines in T cells from old mice with the time of stimulation, suggesting the existence of different mechanisms of post-transcriptional regulation in young and old mice. We found that the IL-2 mRNA level in T cells from young but not from old mice increased up to 6- to 10-fold by addition of cycloheximide (CHX) while the stability of IL-2 mRNA is not affected. We then looked for IL-2 inducible **inhibitory** factors in T cells from young and old mice and demonstrated the presence of Nil-2-a, a **zinc finger** protein which negatively controls IL-2 gene transcription in human cells. This protein could be detected in T cells from both young and old mice, yet, in the presence of CHX, its binding activity was reduced by 75% in T cells from young but not from old mice. These findings show that Nil-2-a accounts for the negative control of IL-2 production in the mouse and explain the reduced IL-2 production in aging.

L6 ANSWER 8 OF 82 MEDLINE

Full-text

AN 1998400433 MEDLINE

DN 98400433 PubMed ID: 9731707

TI Stat 5b and the orphan nuclear receptors regulate expression of the alpha2-macroglobulin (alpha2M) gene in rat ovarian granulosa cells.

AU Dajee M; Fey G H; Richards J S

CS Department of Cell Biology, Baylor College of Medicine, Houston, Texas 77030, USA.

SO MOLECULAR ENDOCRINOLOGY, (1998 Sep) 12 (9) 1393-409.
Journal code: NGZ; 8801431. ISSN: 0888-8809.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199811

ED Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981125

AB Alpha2-macroglobulin (alpha2M) is a serine protease inhibitor and cytokine inactivator associated with inflammation and tissue remodeling. The gene encoding this protein is selectively induced in the rat corpus luteum by the luteotropic hormone and cytokine, PRL. The promoter of the alpha2M gene contains **two regulatory** regions that bind a diverse set of transcription factors and confer functional activity in ovarian granulosa-luteal cells. The PRL response element (PRLRE) binds PRL-activated (tyrosine-phosphorylated) signal transducers and activators of transcription (Stat 5b and Stat 5a). 5'-Deletion of the Stat-binding sites or mutation of either one or both of these sites within the context of the intact promoter abolished PRL inducibility of alpha2M

promoter-reporter constructs in granulosa-luteal cells. Cotransfection with a vector expressing a dominant negative, truncated form of Stat 5b abolished PRL-induced activation of a2M transgenes. 5'-Deletion of the Stat-binding sites abolished all promoter-reporter activity in response to PRL. Internal deletion of a second functional domain 3' of the PRLRE also abolished PRL inducibility and markedly reduced basal activity, indicating that functional interactions between these two regions might occur. The 3'-region was shown to bind orphan members of the nuclear receptor superfamily, steroidogenic factor 1 (SF-1) and chicken ovalbumin upstream promoter-transcription factor (COUP-TF) and has been called the orphan receptor response element (ORRE). When site-specific mutations were made in either the SF-1 -binding site or the two COUP-TF direct repeat (DR1 and DR2) binding sites in the context of the intact promoter, specific changes in the functional activity of this novel region of the alpha2M promoter were observed. Mutation of the SF-1 site drastically reduced basal activity of the alpha2M promoter. Mutation of the COUP-TF sites caused the basal activity of the alpha2M promoter to increase markedly. Neither mutation altered the PRL inducibility of these constructs. Lastly, differentiation of cultured granulosa cells was required for functional activity of both the PRLRE and the ORRE. Collectively, these results document for the first time that Stat 5b, SF-1, and COUP-TF each exert specific effects on the function of the alpha2M promoter: basal activity is controlled by the balance of SF-1 (positive) and COUP-TF (negative) activities and PRL inducibility is mediated by activation of Stat 5b. These results add alpha2M to the list of nonsteroidal genes regulated by SF-1 in the gonads and provide the first evidence that COUP-TF has a specific role in regulating ovarian gene activity. In addition, the ORRE and PRLRE act independently of, rather than synergistically with, each other to regulate basal and PRL-induced expression of alpha2M in ovarian luteal cells.

L6 ANSWER 9 OF 82 MEDLINE DUPLICATE 7
Full-text
AN 1998381937 MEDLINE
DN 98381937 PubMed ID: 9717837
TI Common mutations in autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy patients of different origins.
AU Scott H S; Heino M; Peterson P; Mittaz L; Lalioti M D; Betterle C; Cohen A; Seri M; Lerone M; Romeo G; Collin P; Salo M; Metcalfe R; Weetman A; Papasavvas M P; Rossier C; Nagamine K; Kudoh J; Shimizu N; Krohn K J; Antonarakis S E
CS Department of Genetics and Microbiology, University of Geneva Medical School, Switzerland.. Hamish.Scott@medecine.unige.ch
SO MOLECULAR ENDOCRINOLOGY, (1998 Aug) 12 (8) 1112-9.
Journal code: NGZ; 8801431. ISSN: 0888-8809.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199810
ED Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981029
AB Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED; OMIM *240300, also called APS 1,) is a rare autosomal recessive disorder that is more frequent in certain isolated populations. It is generally characterized by two of the three major clinical symptoms that may be present, Addison's disease and/or hypoparathyroidism and/or chronic mucocutaneous candidiasis. Patients may also have a number of other clinical symptoms including chronic gastritis, gonadal failure, and

rarely, autoimmune thyroid disease and insulin-dependent diabetes mellitus. We and others have recently identified the gene for APECED, which we termed AIRE (for autoimmune regulator). AIRE is expressed in thymus, lymph nodes, and fetal liver and encodes a protein containing motifs suggestive of a transcriptional **regulator**, including **two zinc finger** motifs (PHD finger), a proline-rich region, and three LXXLL motifs. Six mutations, including R257X, the predominant Finnish APECED allele, have been defined. R257X was also observed in non-Finnish APECED patients occurring on different chromosomal haplotypes suggesting different mutational origins. Here we present mutation analyses in an extended series of patients, mainly of Northern Italian origin. We have detected 12 polymorphisms, including one amino acid substitution, and two additional mutations, R203X and X546C, in addition to the previously described mutations, R257X, 1096-1097insCCTG, and a 13-bp deletion (1094-1106del). R257X was also the common mutation in the Northern Italian patients (10 of 18 alleles), and 1094-1106del accounted for 5 of 18 Northern Italian alleles. Both R257X and 1094-1106del were both observed in patients of four different geo-ethnic origins, and both were associated with multiple different haplotypes using closely flanking polymorphic markers showing likely multiple mutation events (six and four, respectively). The identification of common AIRE mutations in different APECED patient groups will facilitate its genetic diagnosis. In addition, the polymorphisms presented provide the tools for investigation of the involvement of AIRE in other autoimmune diseases, particularly those affecting the endocrine system.

L6 ANSWER 10 OF 82 MEDLINE

Full-text

AN 1998161785 MEDLINE

DN 98161785 PubMed ID: 9494074

TI Lysophosphatidic acid-mediated signal-transduction pathways involved in the induction of the early-response genes prostaglandin G/H synthase-2 and Egr-1: a critical role for the mitogen-activated protein kinase p38 and for Rho proteins.

AU Reiser C O; Lanz T; Hofmann F; Hofer G; Rupprecht H D; Goppelt-Strube M

CS Medizinische Klinik IV, Universitat Erlangen-Nurnberg, Loschgestr. 8, D-91054 Erlangen, Germany.

SO BIOCHEMICAL JOURNAL, (1998 Mar 15) 330 (Pt 3) 1107-14.

Journal code: 9YO; 2984726R. ISSN: 0264-6021.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199805

ED Entered STN: 19980529

Last Updated on STN: 20000303

Entered Medline: 19980521

AB During inflammatory processes of the kidney, lesions of the glomerulus lead to aggregation of thrombocytes and infiltration of macrophages, which can release bioactive mediators. One of these important signalling molecules is lysophosphatidic acid (LPA). Incubation of rat mesangial cells with LPA induced mRNA and protein expression of the early-response genes pghs-2 (for prostaglandin G/H synthase-2/cyclo-oxygenase-2) and egr-1. As shown by antisense experiments, induction of egr-1 was related to the strong mitogenic effect of LPA. LPA-mediated gene expression was inhibited by pertussis toxin, indicating coupling to G-proteins of the Gi family. Specific inhibition of proteins of the small G-protein subfamily Rho with toxin B from Clostridium difficile led to changes in mesangial cell morphology without induction of apoptosis. LPA-mediated expression of pghs-2 and egr-1 was reduced to base-line levels by toxin B, indicating a

role for Rho proteins in LPA-mediated gene induction. Of the two mitogen-activated protein kinase (MAPK) pathways investigated, the MAPK kinase-extracellular signal-regulated kinase pathway was involved in the induction of both pghs-2 and egr-1 mRNA expression, as shown by the inhibitory effect of PD98059. Activation of the MAPK p38, however, was only related to pghs-2 expression, whereas egr-1 expression was not affected by treatment of mesangial cells with the specific inhibitor SB203580. Taken together our data provide evidence that LPA-mediated activation of MAPK kinase and Rho proteins leads to the induction of the functionally distinct early-response genes pghs-2 and egr-1, whereas activation of MAPK p38 revealed considerable differences between the **regulation** of these **two** genes.

=> d his

(FILE 'HOME' ENTERED AT 20:16:28 ON 10 DEC 2001)

FILE 'MEDLINE, BIOSIS' ENTERED AT 20:18:21 ON 10 DEC 2001

L1 12117 S ZINC FINGER
L2 590 S L1 AND (TWO OR 2) (2A) (DOMAIN)
L3 803 S L1 AND ((TWO OR 2) (2A) (DOMAIN OR REGULAT? OR INHIBIT?))
L4 225 S L1 AND ((TWO OR 2) (2A) (REGULAT? OR INHIBIT?))
L5 133 S L4 AND PY<1999
L6 82 DUPLICATE REMOVE L5 DUPLICATE REMOVE L5 (51 DUPLICATES REMOVE

=> s (zinc finger) (5A) ((two or 2) (regulat? or inhibit?))

MISSING OPERATOR 2) (REGULAT?

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=> s (zinc finger) (5A) ((two or 2) (2A) (regulat? or inhibit?))

L7 26 (ZINC FINGER) (5A) ((TWO OR 2) (2A) (REGULAT? OR INHIBIT?))

=> duplicate remove l7

DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L7

L8 18 DUPLICATE REMOVE L7 (8 DUPLICATES REMOVED)

=> d 1-18 bib ab

L8 ANSWER 1 OF 18 MEDLINE

Full-text

AN 2001574809 IN-PROCESS

DN 21538881 PubMed ID: 11533054

TI The Autoimmune Regulator (AIRE) Is a DNA-binding Protein.

AU Kumar P G; Laloraya M; Wang C Y; Ruan Q G; Davoodi-Semiromi A; Kao K J; She J X

CS Department of Pathology, Immunology, and Laboratory Medicine, Center for Mammalian Genetics and Diabetes Center of Excellence, College of Medicine, University of Florida, Gainesville, Florida 32610.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Nov 2) 276 (44) 41357-64.
Journal code: HIV; 2985121R. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS IN-PROCESS; NONINDEXED; Priority Journals

ED Entered STN: 20011030

Last Updated on STN: 20011030

AB The autoimmune regulator (AIRE) protein is a putative transcription **regulat r** with **two** plant homeodomain-type **zinc fingers**, a putative DNA-binding domain (SAND), and four nuclear receptor binding LXXLL motifs. We have shown here that in vitro, recombinant AIRE can form homodimers and homotetramers that were also detected in thymic protein extracts. Recombinant AIRE also oligomerizes spontaneously upon phosphorylation by cAMP dependent protein kinase A or protein kinase C. Similarly, thymic AIRE protein is phosphorylated at the tyrosine and serine/threonine residues. AIRE dimers and tetramers, but not the monomers, can bind to G-doublents with the ATTGGTTA motif and the TTATTA-box. Competition assays revealed that sequences with one TTATTA motif and two tandem repeats of ATTGGTTA had the highest binding affinity. These findings demonstrate that AIRE is an important DNA binding molecule involved in immune regulation.

L8 ANSWER 2 OF 18 MEDLINE

DUPLICATE 1

Full-text

AN 2001324631 MEDLINE

DN 21181828 PubMed ID: 11285234

TI A family of snail-related **zinc finger** proteins **regulates two** distinct and parallel mechanisms that mediate Drosophila neuroblast asymmetric divisions.

AU Cai Y; Chia W; Yang X

CS Institute of Molecular and Cell Biology, 30 Medical Drive, Singapore.

SO EMBO JOURNAL, (2001 Apr 2) 20 (7) 1704-14.
Journal code: EMB; 8208664. ISSN: 0261-4189.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200106

ED Entered STN: 20010611

Last Updated on STN: 20010611

Entered Medline: 20010607

AB Three snail family genes snail, escargot and wormiu, encode related zinc finger transcription factors that mediate Drosophila central nervous system (CNS) development. We show that simultaneous removal of all three genes causes defective neuroblast asymmetric divisions; inscuteable transcription/translation is delayed/suppressed in the segmented CNS. Further more, defects in localization of cell fate determinants and orientation of the mitotic spindle in dividing neuroblasts are much stronger than those associated with inscuteable loss of function. In inscuteable neuroblasts, cell fate determinants are mislocalized during prophase and metaphase, yet during anaphase and telophase the great majority of mutant neuroblasts localize these determinants as cortical crescents overlying one of the spindle poles. This phenomenon, known as 'telophase rescue', does not occur in the absence of the snail family genes; moreover, in contrast to inscuteable mutants, mitotic spindle orientation is completely randomized. Our data provide further evidence for the existence of two distinct asymmetry-controlling mechanisms in neuroblasts both of which require snail family gene function: an inscuteable-dependent mechanism that functions throughout mitosis and an inscuteable-independent mechanism that acts during anaphase/telophase.

L8 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS

Full-text

AN 2001:68805 BIOSIS

DN PREV200100068805

TI Retinoic acid inhibits BTEB2 gene expression and its function in vascular smooth muscle cells: The potential role of BTEB2 in retinoic acid-mediated inhibition of neointimal formation after balloon injury.

AU Kowase, Keiko Kawai (1); Kurabayashi, Masahiko (1)
CS (1) Gunma Univ Sch of Medicine, Maebashi, Gunma Japan
SO Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.247.
print.
Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans,
Louisiana, USA November 12-15, 2000
ISSN: 0009-7322.
DT Conference
LA English
SL English

L8 ANSWER 4 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS

Full-text

AN 1999:377915 BIOSIS
DN PREV199900377915
TI Negative cross-talk between hematopoietic regulators: GATA proteins
repress PU.1.
AU Zhang, Pu; Behre, Gerhard; Pan, Jing; Iwama, Atsushi; Wara-Aswapati,
Nawarat; Radomska, Hanna S.; Auron, Philip E.; Tenen, Daniel G. (1); Sun,
Zijie
CS (1) Harvard Institutes of Medicine, 77 Avenue Louis Pasteur, Room 954,
Boston, MA, 02115 USA
SO Proceedings of the National Academy of Sciences of the United States of
America, (July 20, 1999) Vol. 96, No. 15, pp. 8705-8710.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB The process through which multipotential hematopoietic cells commit to
distinct lineages involves the induction of specific transcription
factors. PU.1 (also known as Spi-1) and GATA-1 are transcription factors
essential for the development of myeloid and erythroid lineages,
respectively. Overexpression of PU.1 and GATA-1 can block differentiation
in lineages in which they normally are down-regulated, indicating that not
only positive but negative regulation of these factors plays a role in
normal hematopoietic lineage development. Here we demonstrate that a
region of the PU.1 Ets domain (the winged helix-turn-helix wing) interacts
with the conserved carboxyl-terminal zinc finger of GATA-1 and GATA-2 and
that GATA proteins inhibit PU.1 transactivation of critical myeloid target
genes. We demonstrate further that GATA inhibits binding of PU.1 to c-Jun,
a critical coactivator of PU.1 transactivation of myeloid promoters.
Finally, PU.1 protein can inhibit both GATA-1 and GATA-2 transactivation
function. Our results suggest that interactions between PU.1 and GATA
proteins play a critical role in the decision of stem cells to commit to
erythroid vs. myeloid lineages.

L8 ANSWER 5 OF 18 MEDLINE

Full-text

AN 2000002891 MEDLINE
DN 20002891 PubMed ID: 10531404
TI Lead inhibition of DNA-binding mechanism of Cys(2)His(2) zinc finger
proteins.
AU Hanas J S; Rodgers J S; Bantle J A; Cheng Y G
CS Department of Biochemistry and Molecular Biology, University of Oklahoma
College of Medicine, Oklahoma City, Oklahoma 73104, USA..
Jay-Hanas@ouhsc.edu
SO MOLECULAR PHARMACOLOGY, (1999 Nov) 56 (5) 982-8.
Journal code: NGR; 0035623. ISSN: 0026-895X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
 FS Priority Journals
 EM 199911
 ED Entered STN: 20000111
 Last Updated on STN: 20000111
 Entered Medline: 19991124

AB The association of lead with chromatin in cells suggests that deleterious metal effects may in part be mediated through alterations in gene function. To elucidate if and how lead may alter DNA binding of cysteine-rich zinc finger proteins, lead ions were analyzed for their ability to alter the DNA binding mechanism of the Cys(2)His(2) zinc finger protein transcription factor IIIA (TFIIIA). As assayed by DNase I protection, the interaction of TFIIIA with the 50-bp internal control region of the 5S ribosomal gene was partially inhibited by 5 microM lead ions and completely inhibited by 10 to 20 microM lead ions. Preincubation of free TFIIIA with lead resulted in DNA-binding inhibition, whereas preincubation of a TFIIIA/5S RNA complex with lead did not result in DNA-binding inhibition. Because 5S RNA binds TFIIIA zinc fingers, this result is consistent with an inhibition mechanism via lead binding to zinc fingers. The complete loss of DNase I protection on the 5S gene indicates the mechanism of inhibition minimally involves the N-terminal fingers of TFIIIA. Inhibition was not readily reversible and occurred in the presence of an excess of beta-mercaptoethanol. Inhibition kinetics were fast, progressing to completion in approximately 5 min. Millimolar concentrations of sulfhydryl-specific arsenic ions were not inhibitory for TFIIIA binding. Micromolar concentrations of lead inhibited DNA binding by Sp1, another Cys(2)His(2) finger protein, but not by the nonfinger protein AP2. **Inhibition of Cys(2)His(2) zinc finger** transcription factors by lead ions at concentrations near those known to have deleterious physiological effects points to new molecular mechanisms for lead toxicity in promoting disease.

L8 ANSWER 6 OF 18 MEDLINE DUPLICATE 2

Full-text

AN 1998434612 MEDLINE
 DN 98434612 PubMed ID: 9756940
 TI The early growth response protein (EGR-1) regulates interleukin-2 transcription by synergistic interaction with the nuclear factor of activated T cells.
 AU Decker E L; Skerka C; Zipfel P F
 CS Research Group of Biomolecular Medicine, Bernhard Nocht Institute for Tropical Medicine, Bernhard-Nocht-Strasse 74, D-20359 Hamburg, Germany.
 SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 9) 273 (41) 26923-30.
 Journal code: HIV; 2985121R. ISSN: 0021-9258.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199811
 ED Entered STN: 19990106
 Last Updated on STN: 19990106
 Entered Medline: 19981102

AB The early growth response-1 gene (EGR-1) is induced by a wide range of stimuli in diverse cell types; however, EGR-1-regulated genes display a highly restricted pattern of expression. Recently, an overlapping Sp1.EGR-1 binding site has been identified within the interleukin-2 (IL-2) gene promoter directly upstream of the binding site for the nuclear factor of activated T cells (NFAT). We used transfection assays to study how the abundantly and constitutively expressed Sp1 protein and the immediate early EGR-1 **zinc finger** protein **regulate** IL-2 gene expression.

Here, we identify EGR-1 as an important activator of the IL-2 gene. In Jurkat T cells, EGR-1 but not Spl acts as a potent coactivator for IL-2 transcription, and in combination with NFATc, EGR-1 increases transcription of an IL-2 reporter construct 200-fold. Electrophoretic mobility shift assays reveal that recombinant EGR-1 and NFATc bind independently to their target sites within the IL-2 promoter, and the presence of both sites on the same DNA molecule is required for EGR-1.NFATc.DNA complex formation. The transcriptional synergy observed here for EGR-1 and NFATc explains how the abundant nuclear factor EGR-1 contributes to the expression of restrictively expressed genes.

L8 ANSWER 7 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS

Full-text

AN 1998:296836 BIOSIS

DN PREV199800296836

TI XRCC1 is specifically associated with poly(ADP-ribose) polymerase and negatively regulates its activity following DNA damage.

AU Masson, Murielle; Niedergang, Claude; Schreiber, Valerie; Muller, Sylviane; Menissier-De Murcia, Josiane; De Murcia, Gilbert (1)

CS (1) Ecole Supérieure Biotechnol. Strasbourg, UPR 9003 Cent. Natl. Rech. Sci., Boulevard S. Brant, F-67400 Illkirch-Graffenstaden France

SO Molecular and Cellular Biology, (June, 1998) Vol. 18, No. 6, pp. 3563-3571.

ISSN: 0270-7306.

DT Article

LA English

AB Poly(ADP-ribose) polymerase (PARP; EC 2.4.2.30) is a zinc-finger DNA-binding protein that detects and signals DNA strand breaks generated directly or indirectly by genotoxic agents. In response to these breaks, the immediate poly(ADP-ribosyl)ation of nuclear proteins involved in chromatin architecture and DNA metabolism converts DNA damage into intracellular signals that can activate DNA repair programs or cell death options. To have greater insight into the physiological function of this enzyme, we have used the two-hybrid system to find genes encoding proteins putatively interacting with PARP. We have identified a physical association between PARP and the base excision repair (BER) protein XRCC1 (X-ray repair cross-complementing 1) in the *Saccharomyces cerevisiae* system, which was further confirmed to exist in mammalian cells. XRCC1 interacts with PARP by its central region (amino acids 301 to 402), which contains a BRCT (BRCA1 C terminus) module, a widespread motif in DNA repair and DNA damage-responsive cell cycle checkpoint proteins. Overexpression of XRCC1 in Cos-7 or HeLa cells dramatically decreases PAR-P activity in vivo, reinforcing the potential protective function of PARP at DNA breaks. Given that XRCC1 is also associated with DNA ligase III via a second BRCT module and with DNA polymerase beta, our results provide strong evidence that PARP is a member of a BER multiprotein complex involved in the detection of DNA interruptions and possibly in the recruitment of XRCC1 and its partners for efficient processing of these breaks in a coordinated manner. The modular organizations of these interactors, associated with small conserved domains, may contribute to increasing the efficiency of the overall pathway.

L8 ANSWER 8 OF 18 MEDLINE

DUPLICATE 3

Full-text

AN 1998381937 MEDLINE

DN 98381937 PubMed ID: 9717837

TI Common mutations in autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy patients of different origins.

AU Scott H S; Heino M; Peterson P; Mittaz L; Lalioti M D; Betterle C; Cohen A; Seri M; Lerone M; Romeo G; Collin P; Salo M; Metcalfe R; Weetman A;

Papasavvas M P; Rossier C; Nagamine K; Kudoh J; Shimizu N; Krohn K J;
Antonarakis S E
CS Department of Genetics and Microbiology, University of Geneva Medical
School, Switzerland.. Hamish.Scott@medecine.unige.ch
SO MOLECULAR ENDOCRINOLOGY, (1998 Aug) 12 (8) 1112-9.
Journal code: NGZ; 8801431. ISSN: 0888-8809.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199810
ED Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981029
AB Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED;
OMIM *240300, also called APS 1,) is a rare autosomal recessive disorder
that is more frequent in certain isolated populations. It is generally
characterized by two of the three major clinical symptoms that may be
present, Addison's disease and/or hypoparathyroidism and/or chronic
mucocutaneous candidiasis. Patients may also have a number of other
clinical symptoms including chronic gastritis, gonadal failure, and
rarely, autoimmune thyroid disease and insulin-dependent diabetes
mellitus. We and others have recently identified the gene for APECED,
which we termed AIRE (for autoimmune regulator). AIRE is expressed in
thymus, lymph nodes, and fetal liver and encodes a protein containing
motifs suggestive of a transcriptional **regulator**, including **two zinc
finger** motifs (PHD finger), a proline-rich region, and three LXXLL
motifs. Six mutations, including R257X, the predominant Finnish APECED
allele, have been defined. R257X was also observed in non-Finnish APECED
patients occurring on different chromosomal haplotypes suggesting
different mutational origins. Here we present mutation analyses in an
extended series of patients, mainly of Northern Italian origin. We have
detected 12 polymorphisms, including one amino acid substitution, and two
additional mutations, R203X and X546C, in addition to the previously
described mutations, R257X, 1096-1097insCCTG, and a 13-bp deletion
(1094-1106del). R257X was also the common mutation in the Northern Italian
patients (10 of 18 alleles), and 1094-1106del accounted for 5 of 18
Northern Italian alleles. Both R257X and 1094-1106del were both observed
in patients of four different geo-ethnic origins, and both were associated
with multiple different haplotypes using closely flanking polymorphic
markers showing likely multiple mutation events (six and four,
respectively). The identification of common AIRE mutations in different
APECED patient groups will facilitate its genetic diagnosis. In addition,
the polymorphisms presented provide the tools for investigation of the
involvement of AIRE in other autoimmune diseases, particularly those
affecting the endocrine system.

L8 ANSWER 9 OF 18 MEDLINE DUPLICATE 4

Full-text

AN 1998099749 MEDLINE
DN 98099749 PubMed ID: 9436984
TI Regulation of POU genes by castor and hunchback establishes layered
compartments in the Drosophila CNS.
AU Kambadur R; Koizumi K; Stivers C; Nagle J; Poole S J; Odenwald W F
CS The Neurogenetics Unit, Laboratory of Neurochemistry, National Institute
of Neurological Disorders and Stroke (NINDS), National Institutes of
Health (NIH), Bethesda, Maryland 20892 USA.
SO GENES AND DEVELOPMENT, (1998 Jan 15) 12 (2) 246-60.
Journal code: FN3; 8711660. ISSN: 0890-9369.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF035264
EM 199803
ED Entered STN: 19980312

Last Updated on STN: 19980312

Entered Medline: 19980305

AB POU transcription factors participate in cell-identity decisions during nervous system development, yet little is known about the regulatory networks controlling their expression. We report all known Drosophila POU genes require castor (cas) for correct CNS expression. drifter and I-POU depend on cas for full expression, whereas pdm-1 and pdm-2 are negatively **regulated**. cas encodes a **zinc finger** protein that shares DNA-binding specificity with another pdm repressor: the gap segmentation gene regulator Hunchback (Hb). Our studies reveal that the embryonic CNS contains sequentially generated neuroblast sublineages that can be distinguished by their expression of either Hb, Pdm-1, or Cas. Hb and Cas may directly silence pdm expression in early and late developing sublineages, given that pdm-1 cis-regulatory DNA contains ≥ 32 Hb/Cas-binding sites and its enhancer(s) are ectopically activated in cas-neuroblasts. In addition, the targeted misexpression of Cas in all neuroblast lineages reduces Pdm-1 expression without altering Hb expression. By ensuring correct POU gene expression boundaries, hb and cas maintain temporal subdivisions in the cell-identity circuitry controlling CNS development.

L8 ANSWER 10 OF 18 MEDLINE

Full-text

AN 1998073564 MEDLINE

DN 98073564 PubMed ID: 9409150

TI Metabolism of sulfur amino acids in Saccharomyces cerevisiae.

AU Thomas D; Surdin-Kerjan Y

CS Centre de Genetique Moleculaire, CNRS, Gif sur Yvette, France.

SO MICROBIOLOGY AND MOLECULAR BIOLOGY REVIEWS, (1997 Dec) 61 (4) 503-32.

Ref: 271

Journal code: CS0; 9706653. ISSN: 1092-2172.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, ACADEMIC)

LA English

FS Priority Journals

EM 199802

ED Entered STN: 19980217

Last Updated on STN: 20000303

Entered Medline: 19980205

AB Sulfur amino acid biosynthesis in Saccharomyces cerevisiae involves a large number of enzymes required for the de novo biosynthesis of methionine and cysteine and the recycling of organic sulfur metabolites. This review summarizes the details of these processes and analyzes the molecular data which have been acquired in this metabolic area. Sulfur biochemistry appears not to be unique through terrestrial life, and S. cerevisiae is one of the species of sulfate-assimilatory organisms possessing a larger set of enzymes for sulfur metabolism. The review also deals with several enzyme deficiencies that lead to a nutritional requirement for organic sulfur, although they do not correspond to defects within the biosynthetic pathway. In S. cerevisiae, the sulfur amino acid biosynthetic pathway is tightly controlled: in response to an increase in the amount of intracellular S-adenosylmethionine (AdoMet), transcription

of the coregulated genes is turned off. The second part of the review is devoted to the molecular mechanisms underlying this regulation. The coordinated response to AdoMet requires two cis-acting promoter elements. One centers on the sequence TCACGTG, which also constitutes a component of all *S. cerevisiae* centromeres. Situated upstream of the sulfur genes, this element is the binding site of a transcription activation complex consisting of a basic helix-loop-helix factor, Cbflp, and two basic leucine zipper factors, Met4p and Met28p. Molecular studies have unraveled the specific functions for each subunit of the Cbflp-Met4p-Met28p complex as well as the modalities of its assembly on the DNA. The Cbflp-Met4p-Met28p complex contains only one transcription activation module, the Met4p subunit. Detailed mutational analysis of Met4p has elucidated its functional organization. In addition to its activation and bZIP domains, Met4p contains two regulatory domains, called the inhibitory region and the auxiliary domain. When the level of intracellular AdoMet increases, the transcription activation function of Met4 is prevented by Met30p, which binds to the Met4 inhibitory region. In addition to the Cbflp-Met4p-Met28p complex, transcriptional **regulation** involves **two zinc finger**-containing proteins, Met31p and Met32p. The AdoMet-mediated control of the sulfur amino acid pathway illustrates the molecular strategies used by eucaryotic cells to couple gene expression to metabolic changes.

L8 ANSWER 11 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS

Full-text

AN 1996:219352 BIOSIS

DN PREV199698775481

TI Inhibition of transcription factor IIIA-DNA interactions by xenobiotic metal ions.

AU Hanas, Jay S. (1); Gunn, C. G.

CS (1) Dep. Biochem. Mol. Biol., Univ. Oklahoma Coll. Med., Oklahoma City, OK 73190 USA

SO Nucleic Acids Research, (1996) Vol. 24, No. 5, pp. 924-930.
ISSN: 0305-1048.

DT Article

LA English

AB Transcription factor IIIA (TFIIIA), a cysteine-rich regulatory protein, is the prototype for the largest known superfamily of eukaryotic transcription factors. Members of the TFIIIA superfamily contain Cys-2His-2 zinc finger domains responsible for nucleic acid binding. Xenobiotic metal ions, which lack known biological function, were previously used as probes for the structure and function of steroid hormone receptors which contain Cys-2Cys-2 zinc finger domains. Structural alterations in cysteine-rich regulatory proteins by such ions in vivo might potentiate carcinogenesis and other disease processes. In the present study cadmium and other xenobiotic metal ions were used to probe the structure and function of TFIIIA. The specific interaction of TFIIIA with the internal control region (ICR) of the 5S RNA gene, as assayed by DNase I protection, was inhibited by Cd-2+ ion concentrations of gtoreq 0.1 mu-M. Aluminum ions were also found to inhibit the TFIIIA-5S RNA gene interaction, albeit at higher concentrations (gtoreq 5 mu-M). Inhibition by either metal ion was not readily reversible. Other xenobiotic metal ions, such as mercury or cesium, were not found to be inhibitory under these conditions. None of these ions at the concentrations used in this study affected the ability of DNase I to digest DNA or restriction enzymes to specifically cleave DNA. Preincubation of TFIIIA bound to 5S RNA with either Cd-2+ or Al-3+ resulted in subsequent DNA binding upon dilution and RNA removal, whereas preincubation of free TFIIIA with the metal ions resulted in inhibition of subsequent DNA binding. Because 5S rRNA also binds the TFIIIA zinc finger domains, these results indicate that the 5S

RNA bound to TFIIIA protects the protein from metal inhibition and implicates the zinc fingers in the inhibition mechanism. The nature of the footprint inhibition indicates that the N-terminal fingers of TFIIIA are affected by the metal ions. Cd-2+ and Al-3+ ions also inhibited the ability of TFIIIA to bind complementary single-stranded DNA and promote renaturation, as measured by Tris-phosphate agarose gel electrophoresis. This gel assay is sensitive to DNA conformation and Al-3+ ions were found to alter the conformation of single- and double-stranded DNA in this assay. The inhibition of TFIIIA function in vitro by xenobiotic metals offers new insights into the structure and function of TFIIIA and TFIIIA-type **zinc finger** proteins. **Inhibition** by Cd-2+ occurs at much lower concentrations than previously observed with steroid hormone receptors and suggests that Cys-2His-2 zinc finger proteins may be especially sensitive to such agents in vivo.

L8 ANSWER 12 OF 18 MEDLINE

DUPLICATE 5

Full-text

AN 95403454 MEDLINE

DN 95403454 PubMed ID: 7673240

TI A regulatory element in the human interleukin 2 gene promoter is a binding site for the zinc finger proteins Sp1 and EGR-1.

AU Skerka C; Decker E L; Zipfel P F

CS Department of Molecular Biology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Sep 22) 270 (38) 22500-6.
Journal code: HIV; 2985121R. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199510

ED Entered STN: 19951026

Last Updated on STN: 19970203

Entered Medline: 19951017

AB Activation of the interleukin 2 (IL-2) gene after antigen recognition is a critical event for T cell proliferation and effector function. Prior studies have identified several transcription factors that contribute to the activity of the IL-2 promoter in stimulated T lymphocytes. Here we describe a novel regulatory element within the IL-2 promoter located immediately upstream of the nuclear factor of activated T cell (NFAT) domain. This region (termed the zinc finger protein binding region (ZIP)) serves as binding site for **two** differently **regulated zinc finger** proteins: the constitutively expressed transcription factor Sp1 and the inducible early growth response protein EGR-1. In unstimulated cells which do not secrete IL-2, only Sp1 binds to this region, while in stimulated IL-2 secreting cells the inducible EGR-1 protein recognizes this element. In Jurkat T cells, the ZIP site serves as an activator for IL-2 gene expression, and a combination of ZIP and NFAT binding sites is required for maximal IL-2 promoter activity. These results suggest a critical role of the ZIP site for IL-2 promoter activity.

L8 ANSWER 13 OF 18 MEDLINE

DUPLICATE 6

Full-text

AN 95374947 MEDLINE

DN 95374947 PubMed ID: 7647035

TI Transforming growth factor alpha **regulation** of **two zinc finger**-containing immediate early response genes in intestine.

AU DuBois R N; Bishop P R; Graves-Deal R; Coffey R J

CS Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee 37232, USA.

NC 1R01 DK47297-O21 (NIDDK)
267
CA46413 (NCI)
+

SO CELL GROWTH AND DIFFERENTIATION, (1995 May) 6 (5) 523-9.
Journal code: AYH; 9100024. ISSN: 1044-9523.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199509

ED Entered STN: 19951005

Last Updated on STN: 19951005

Entered Medline: 19950925

AB The epithelium lining the intestine undergoes rapid and continuous renewal. Growth factors play a role in intestinal epithelial growth regulation in vitro and in vivo. In this study, transforming growth factor alpha (TGF alpha) is shown to act as a mitogen and induce the expression of two zinc finger-containing immediate early genes [Zif268 (zinc finger protein 268) and Nup475 (nuclear protein 475)] in rat intestinal epithelial (RIE-1) cells in culture. These two gene products were initially isolated from serum-treated fibroblasts and represent growth-stimulated transcription factors. In TGF alpha-treated RIE-1 cells, nuclear run-on experiments demonstrate that TGF alpha induction of these two genes is regulated predominantly at the level of gene transcription. Utilizing in situ hybridization techniques, we show that systemic administration of TGF alpha induces expression of these two genes in the rat intestine. The predominant expression of zif268 is observed in the proliferative crypt compartment, whereas nup475 expression is concentrated in the postmitotic luminal compartment. These studies demonstrate that two immediate early genes, Nup475 and Zif268, are induced in intestinal epithelium in vitro and in vivo and thus may play a role in intestinal epithelial growth and/or differentiation.

L8 ANSWER 14 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS

Full-text

AN 1996:88431 BIOSIS

DN PREV199698660566

TI A novel regulatory element in the human IL-2 gene promoter is a binding site for **two** differently **regulated zinc-finger** proteins.

AU Decker, Eva L. (1); Skerka, Christine; Zipfel, Peter F.

CS (1) Bernhard Nocht Inst. Tropical Med., Bernhard-Nocht-Strasse 74, 20359 Hamburg Germany

SO Biological Chemistry Hoppe-Seyler, (1995) Vol. 376, No. SPEC. SUPPL., pp. S92.

Meeting Info.: Fall Meeting of the Gesellschaft fuer Biologische Chemie Hannover, Germany September 11-13, 1995

ISSN: 0177-3593.

DT Conference

LA English

L8 ANSWER 15 OF 18 MEDLINE

Full-text

AN 94344075 MEDLINE

DN 94344075 PubMed ID: 8065303

TI Nuclear c-Myc plays an important role in the cytotoxicity of tumor necrosis factor alpha in tumor cells.

AU Janicke R U; Lee F H; Porter A G

CS Institute of Molecular and Cell Biology, National University of Singapore.

SO MOLECULAR AND CELLULAR BIOLOGY, (1994 Sep) 14 (9) 5661-70.

Journal code: NGY; 8109087. ISSN: 0270-7306.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199409

ED Entered STN: 19941005

Last Updated on STN: 19970203

Entered Medline: 19940919

AB The phosphoprotein c-Myc has the potential to kill cells by apoptosis. To investigate whether c-Myc is involved in tumor necrosis factor alpha (TNF-alpha)-mediated cell killing, we have examined two HeLa cell lines (D98 and H21) which show dramatic differences in their susceptibilities to TNF-alpha cytotoxicity. Northern (RNA) blot analyses showed that there were no significant differences between these cell lines in basal or TNF-alpha-induced mRNA expression for a variety of proteins, including manganous superoxide dismutase, A20 **zinc finger** protein, plasminogen activator **inhibitor** type 2, and hsp70, all of which are known to influence the susceptibility of certain cells to TNF-alpha killing. On the other hand, there was a dramatic increase in c-Myc mRNA expression in TNF-alpha-sensitive D98 cells, but not in TNF-alpha-resistant H21 cells, which was only observed when the cells were treated with cycloheximide. Western blot (immunoblot) analyses revealed that even in the absence of TNF-alpha or cycloheximide, c-Myc was detectable only in nuclear extracts of TNF-alpha-sensitive D98 cells, implying a role for preexisting c-Myc in TNF-alpha killing. In support of this interpretation, a c-myc antisense oligonucleotide specifically inhibited the TNF-alpha killing of D98 cells, provided that the oligonucleotide was added 6 h prior to TNF-alpha treatment. Either dexamethasone treatment or transient expression of c-myc antisense cDNA fragments decreased nuclear c-Myc in D98 cells and rendered the cells more resistant to TNF-alpha cytotoxicity. Nuclear c-Myc was also detectable in a TNF-alpha-sensitive human HT-1080 fibrosarcoma cell line, but it was undetectable in a derivative of HT-1080 (SS-HT-1080) known to be resistant to TNF-alpha killing because of overexpression of plasminogen activator inhibitor type 2. HT-1080 cells transfected with antisense c-myc cDNA had significantly less nuclear c-Myc and were resistant to TNF-alpha cytotoxicity. Together, these data indicate that a nuclear transcription factor, c-Myc, plays an important role in sensitizing two different tumor cell types to TNF-alpha cytotoxicity.

L8 ANSWER 16 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS

Full-text

AN 1994:452076 BIOSIS

DN PREV199497465076

TI Nuclear c-Myc plays an important role in the cytotoxicity of tumor necrosis factor alpha in tumor cells.

AU Janicke, Reiner U. (1); Lee, Fiona H. H.; Porter, Alan G.

CS (1) Protein Eng. Lab., Inst. Mol. and Cell Biol., National Univ. Singapore, 10 Kent Ridge Crescent, Singapore 0511 Singapore

SO Molecular and Cellular Biology, (1994) Vol. 14, No. 9, pp. 561-5670. ISSN: 0270-7306.

DT Article

LA English

AB The phosphoprotein c-Myc has the potential to kill cells by apoptosis. To investigate whether c-Myc is involved in tumor necrosis factor alpha (TNF-alpha)-mediated cell killing, we have examined two HeLa cell lines (D98 and H21) which show dramatic differences in their susceptibilities to TNF-alpha cytotoxicity. Northern (RNA) blot analyses showed that there were no significant differences between these cell lines in basal or TNF-alpha-induced mRNA expression for a variety of proteins, including

manganous superoxide dismutase, A20 **zinc finger** protein, plasminogen activator **inhibitor** type 2, and hsp70, all of which are known to influence the susceptibility of certain cells to TNF-alpha killing. On the other hand, there was a dramatic increase in c-Myc mRNA expression in TNF-alpha-sensitive D98 cells, but not in TNF-alpha-resistant H21 cells, which was only observed when the cells were treated with cycloheximide. Western blot (immunoblot) analyses revealed that even in the absence of TNF-alpha or cycloheximide, c-Myc was detectable only in nuclear extracts of TNF-alpha-sensitive D98 cells, implying a role for preexisting c-Myc in TNF-alpha killing. In support of this interpretation, a c-myc antisense oligonucleotide specifically inhibited the TNF-alpha killing of D98 cells, provided that the oligonucleotide was added 6 h prior to TNF-alpha treatment. Either dexamethasone treatment or transient expression of c-myc antisense cDNA fragments decreased nuclear c-Myc in D98 cells and rendered the cells more resistant to TNF-alpha cytotoxicity. Nuclear c-Myc was also detectable in a TNF-alpha-sensitive human HT-1080 fibrosarcoma cell line, but it was undetectable in a derivative of HT-1080 (SS-HT-1080) known to be resistant to TNF-alpha killing because of overexpression of plasminogen activator inhibitor type 2. HT-1080 cells transfected with antisense c-myc cDNA had significantly less nuclear c-Myc and were resistant to TNF-alpha cytotoxicity. Together, these data indicate that a nuclear transcription factor, c-Myc, plays an important role in sensitizing two different tumor cell types to TNF-alpha cytotoxicity.

L8 ANSWER 17 OF 18 MEDLINE DUPLICATE 7

Full-text

AN 93052298 MEDLINE
 DN 93052298 PubMed ID: 1427828
 TI The TCF8 gene encoding a zinc finger protein (Nil-2-a) resides on human chromosome 10p11.2.
 AU Williams T M; Montoya G; Wu Y; Eddy R L; Byers M G; Shows T B
 CS Department of Pathology, University of New Mexico School of Medicine, Albuquerque 87131.
 NC CA-54428 (NCI)
 HD-05196 (NICHD)
 HG-00333 (NHGRI)
 SO GENOMICS, (1992 Sep) 14 (1) 194-6.
 Journal code: GEN; 8800135. ISSN: 0888-7543.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199212
 ED Entered STN: 19930122
 Last Updated on STN: 19980206
 Entered Medline: 19921222
 AB The TCF8 gene encodes a **zinc finger** protein (Nil-2-a). Nil-2-a **inhibits** T-lymphocyte-specific interleukin 2 (IL2) gene expression by binding to a negative regulatory domain 100 nucleotides 5' of the IL2 transcription start site. Southern hybridization and somatic cell hybrids are used to demonstrate that the murine and human genomes contain related genes for Nil-2-a. TCF8 resides on human chromosome 10. Fluorescent in situ hybridization is employed to localize TCF8 to 10p11.2.

L8 ANSWER 18 OF 18 MEDLINE DUPLICATE 8

Full-text

AN 92108424 MEDLINE
 DN 92108424 PubMed ID: 1840704
 TI Identification of a **zinc finger** protein that **inhibits** IL-2 gene expression.

AU Williams T M; Moolten D; Burlein J; Romano J; Bhaerman R; Godillot A;
Mellon M; Rauscher F J 3rd; Kant J A
CS Department of Pathology, School of Medicine, University of New Mexico,
Albuquerque 87131.
NC AI23879 (NIAID)
CA23413 (NCI)
CA54428 (NCI)
+
SO SCIENCE, (1991 Dec 20) 254 (5039) 1791-4.
Journal code: UJ7; 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M76239; GENBANK-M76240; GENBANK-M76241; GENBANK-M76242;
GENBANK-M76243; GENBANK-M76244; GENBANK-M81699; GENBANK-M83741;
GENBANK-M83742; GENBANK-S70464
EM 199202
ED Entered STN: 19920302
Last Updated on STN: 19920302
Entered Medline: 19920212
AB Transient activation of the interleukin-2 (IL-2) gene after antigen
recognition by T lymphocytes is crucial for subsequent T cell
proliferation and differentiation. Several IL-2 gene regulatory elements
and binding factors necessary for activation of the IL-2 gene have been
defined. However, little is known about negative regulation of IL-2
expression, which is likely to be important in the rapid shut-off of IL-2
transcription. A nucleotide sequence element (NRE-A) that negatively
regulates IL-2 expression has been identified within the IL-2 gene. T cell
nuclear extracts contained an NRE-A binding activity. A complementary DNA
was isolated that encodes a zinc finger-containing protein that suppressed
IL-2 gene expression. The observation of negative regulation of the
immunoglobulin heavy chain gene enhancer by an element similar to NRE-A
suggests that related proteins may regulate multiple immune response
genes.

=> s zinc finger and liposom?

L9 10 ZINC FINGER AND LIPOSOM?

=> duplicate remove l9

DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L9

L10 8 DUPLICATE REMOVE L9 (2 DUPLICATES REMOVED)

=> d 1-8 bib ab

L10 ANSWER 1 OF 8 MEDLINE

Full-text

AN 2001406027 MEDLINE

DN 21349701 PubMed ID: 11456498

TI High-affinity binding of a FYVE domain to phosphatidylinositol 3-phosphate
requires intact phospholipid but not FYVE domain oligomerization.

AU Sankaran V G; Klein D E; Sachdeva M M; Lemmon M A

CS Department of Biochemistry and Biophysics, University of Pennsylvania
School of Medicine, Philadelphia, Pennsylvania 19104, USA.

NC GM56846 (NIGMS)

SO BIOCHEMISTRY, (2001 Jul 24) 40 (29) 8581-7.

Journal code: A0G; 0370623. ISSN: 0006-2960.

CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200110
 ED Entered STN: 20011008
 Last Updated on STN: 20011008
 Entered Medline: 20011004
 AB FYVE domains are small **zinc-finger**-like domains found in many proteins that are involved in regulating membrane traffic and have been shown to bind specifically to phosphatidylinositol 3-phosphate (PtdIns-3-P). FYVE domains are thought to recruit PtdIns-3-P effectors to endosomal locations in vivo, where these effectors participate in controlling endosomal maturation and vacuolar protein sorting. We have compared the characteristics of PtdIns-3-P binding by the FYVE domain from Hrs-1 (the hepatocyte growth factor-regulated tyrosine kinase substrate) with those of specific phosphoinositide binding by Pleckstrin homology (PH) domains. Like certain PH domains (such as that from phospholipase C-delta(1)), the Hrs-1 FYVE domain specifically recognizes a single phosphoinositide. However, while phosphoinositide binding by highly specific PH domains is driven almost exclusively by interactions with the lipid headgroup, this is not true for the Hrs-1 FYVE domain. The phospholipase C-delta(1) PH domain shows a 10-fold preference for binding isolated headgroup over its preferred lipid (phosphatidylinositol 4,5-bisphosphate) in a membrane, while the Hrs-1 FYVE domain greatly prefers (more than 50-fold) intact lipid in a bilayer over the isolated headgroup (inositol 1,3-bisphosphate). By contrast with reports for certain PH domains, we find that this preference for membrane binding over interaction with soluble lipid headgroups does not require FYVE domain oligomerization.

L10 ANSWER 2 OF 8 MEDLINE

Full-text

AN 2001158605 MEDLINE
 DN 21108344 PubMed ID: 11161217
 TI Role of the ENTH domain in phosphatidylinositol-4,5-bisphosphate binding and endocytosis.
 CM Comment in: Science. 2001 Feb 9;291(5506):993-4
 AU Itoh T; Koshiba S; Kigawa T; Kikuchi A; Yokoyama S; Takenawa T
 CS Department of Biochemistry, Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan.
 SO SCIENCE, (2001 Feb 9) 291 (5506) 1047-51.
 Journal code: UJ7; 0404511. ISSN: 0036-8075.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200103
 ED Entered STN: 20010404
 Last Updated on STN: 20010404
 Entered Medline: 20010322
 AB Endocytic proteins such as epsin, AP180, and Hip1R (Sla2p) share a conserved modular region termed the epsin NH2-terminal homology (ENTH) domain, which plays a crucial role in clathrin-mediated endocytosis through an unknown target. Here, we demonstrate a strong affinity of the ENTH domain for phosphatidylinositol-4,5-bisphosphate [PtdIns(4,5)P2]. With nuclear magnetic resonance analysis of the epsin ENTH domain, we determined that a cleft formed with positively charged residues contributed to phosphoinositide binding. Overexpression of a mutant, epsin Lys76 --> Ala76, with an ENTH domain defective in phosphoinositide binding, blocked epidermal growth factor internalization in COS-7 cells.

Thus, interaction between the ENTH domain and PtdIns(4,5)P₂ is essential for endocytosis mediated by clathrin-coated pits.

L10 ANSWER 3 OF 8 MEDLINE

DUPLICATE 1

Full-text

AN 2001517166 IN-PROCESS
DN 21448129 PubMed ID: 11563980
TI FYVE **zinc-finger** proteins in the plant model *Arabidopsis thaliana*: identification of PtdIns3P-binding residues by comparison of classic and variant FYVE domains.
AU Jensen R B; La Cour T; Albrethsen J; Nielsen M; Skriver K
CS Institute of Molecular Biology, University of Copenhagen, Oster Farimagsgade 2A, 1353 Copenhagen K, Denmark.
SO BIOCHEMICAL JOURNAL, (2001 Oct 1) 359 (Pt 1) 165-73.
Journal code: 9YO; 2984726R. ISSN: 0264-6021.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20010924
Last Updated on STN: 20010924
AB Classic FYVE **zinc-finger** domains recognize the phosphoinositide signal PtdIns3P and share the basic (R/K)(1)(R/K)HHCR(6) (single-letter amino acid codes) consensus sequence. This domain is present in predicted PtdIns3P 5-kinases and lipases from *Arabidopsis thaliana*. Other *Arabidopsis* proteins, named PRAF, consist of a pleckstrin homology (PH) domain, a regulator of chromosome condensation (RCC1) guanine nucleotide exchange factor repeat domain, and a variant FYVE domain containing an Asn residue and a Tyr residue at positions corresponding to the PtdIns3P-interacting His(4) and Arg(6) of the basic motif. Dot-blot and **liposome**-binding assays were used in vitro to examine the phospholipid-binding ability of isolated PRAF domains. Whereas the PH domain preferentially bound PtdIns(4,5)P₂, the variant FYVE domain showed a weaker charge-dependent binding of phosphoinositides. In contrast, specificity for PtdIns3P was obtained by mutagenic conversion of the variant into a classic FYVE domain (Asn(4),Tyr(6)-->His(4),Arg(6)). Separate substitutions of the variant residues were not sufficient to impose preferential binding of PtdIns3P, suggesting a co-operative effect of these residues in binding. A biochemical function for PRAF was indicated by its ability to catalyse guanine nucleotide exchange on some of the small GTPases of the Rab family, permitting a discussion of the biological roles of plant FYVE proteins and their regulation by phosphoinositides.

L10 ANSWER 4 OF 8 MEDLINE

DUPLICATE 2

Full-text

AN 2001101648 MEDLINE
DN 21070549 PubMed ID: 11202441
TI Promiscuous and specific phospholipid binding by domains in ZAC, a membrane-associated *Arabidopsis* protein with an ARF GAP **zinc finger** and a C2 domain.
AU Jensen R B; Lykke-Andersen K; Frandsen G I; Nielsen H B; Haseloff J; Jespersen H M; Mundy J; Skriver K
CS Institute of Molecular Biology, University of Copenhagen, Denmark.
SO PLANT MOLECULAR BIOLOGY, (2000 Dec) 44 (6) 799-814.
Journal code: A6O. ISSN: 0167-4412.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

OS GENBANK-AF177381; GENBANK-AF184144; GENBANK-AF184145; GENBANK-AF184146
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201
AB Arabidopsis proteins were predicted which share an 80 residue **zinc finger** domain known from ADP-ribosylation factor GTPase-activating proteins (ARF GAPs). One of these is a 37 kDa protein, designated ZAC, which has a novel domain structure in which the N-terminal ARF GAP domain and a C-terminal C2 domain are separated by a region without homology to other known proteins. Zac promoter/beta-glucuronidase reporter assays revealed highest expression levels in flowering tissue, rosettes and roots. ZAC protein was immuno-detected mainly in association with membranes and fractionated with Golgi and plasma membrane marker proteins. ZAC membrane association was confirmed in assays by a fusion between ZAC and the green fluorescence protein and prompted an analysis of the in vitro phospholipid-binding ability of ZAC. Phospholipid dot-blot and **liposome**-binding assays indicated that fusion proteins containing the ZAC-C2 domain bind anionic phospholipids non-specifically, with some variance in Ca²⁺ and salt dependence. Similar assays demonstrated specific affinity of the ZAC N-terminal region (residues 1-174) for phosphatidylinositol 3-monophosphate (PI-3-P). Binding was dependent in part on an intact **zinc finger** motif, but proteins containing only the **zinc finger** domain (residues 1-105) did not bind PI-3-P. Recombinant ZAC possessed GTPase-activating activity on Arabidopsis ARF proteins. These data identify a novel PI-3-P-binding protein region and thereby provide evidence that this phosphoinositide is recognized as a signal in plants. A role for ZAC in the regulation of ARF-mediated vesicular transport in plants is discussed.

L10 ANSWER 5 OF 8 MEDLINE

Full-text

AN 1999321916 MEDLINE
DN 99321916 PubMed ID: 10391930
TI Interplay of C1 and C2 domains of protein kinase C-alpha in its membrane binding and activation.
AU Medkova M; Cho W
CS Department of Chemistry, University of Illinois, Chicago, Illinois 60607-7061, USA.
NC GM53987 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Jul 9) 274 (28) 19852-61.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
ED Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990805
AB The regulatory domain of conventional protein kinase C (PKC) contains two membrane-targeting modules, the C2 domain that is responsible for Ca²⁺-dependent membrane binding of protein, and the C1 domain composed of two cysteine-rich **zinc fingers** (C1a and C1b) that bind diacylglycerols and phorbol esters. To understand the individual roles and the interplay of the C1 and C2 domains in the membrane binding and activation of PKC, we functionally expressed isolated C1 and C2 domains of PKC-alpha and measured their vesicle binding and monolayer penetration. Results indicate that the C2 domain of PKC-alpha is responsible for the initial Ca²⁺- and phosphatidylserine-dependent electrostatic membrane binding of PKC-alpha,

whereas the C1 domain is involved in subsequent membrane penetration and diacylglycerol binding, which eventually lead to enzyme activation. To determine the roles of individual **zinc fingers** in the C1 domain, we also mutated hydrophobic residues in the Cla (Trp58 and Phe60) and Clb (Tyr123 and Leu125) domains of the native PKC-alpha molecule and measured the effects of mutations on vesicle binding, enzyme activity and monolayer penetration. Results show that the hydrophobic residues in the Cla domain are essential for the membrane penetration and activation of PKC-alpha, whereas those in the Clb domain are not directly involved in these processes. Based on these results in conjunction with our previous structure-function studies of the C2 domain (Medkova, M., and Cho, W. (1998) J. Biol. Chem. 273, 17544-17552), we propose a mechanism for the in vitro membrane binding and activation of conventional PKC that accounts for the temporal and spatial sequences of PKC activation.

L10 ANSWER 6 OF 8 MEDLINE

Full-text

AN 1999322673 MEDLINE
 DN 99322673 PubMed ID: 10394369
 TI Phosphatidylinositol 3-phosphate recognition by the FYVE domain.
 AU Kutateladze T G; Ogburn K D; Watson W T; de Beer T; Emr S D; Burd C G; Overduin M
 CS Department of Pharmacology, University of Colorado Health Sciences Center, Denver 80262, USA.
 SO MOLECULAR CELL, (1999 Jun) 3 (6) 805-11.
 Journal code: C5E; 9802571. ISSN: 1097-2765.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199907
 ED Entered STN: 19990730
 Last Updated on STN: 19990730
 Entered Medline: 19990716
 AB Recognition of phosphatidylinositol 3-phosphate (PtdIns(3)P) is crucial for a broad range of cellular signaling and membrane trafficking events regulated by phosphoinositide (PI) 3-kinases. PtdIns(3)P binding by the FYVE domain of human early endosome autoantigen 1 (EEA1), a protein implicated in endosome fusion, involves two beta hairpins and an alpha helix. Specific amino acids, including those of the FYVE domain's conserved RRHHCRCGNIF motif, contact soluble and micelle-embedded lipid and provide specificity for PtdIns(3)P over PtdIns(5)P and PtdIns, as shown by heteronuclear magnetic resonance spectroscopy. Although the FYVE domain relies on a zinc-binding motif reminiscent of RING fingers, it is distinguished by ovel structural features and its ptdIns(3)P-binding site.

L10 ANSWER 7 OF 8 MEDLINE

Full-text

AN 1998361230 MEDLINE
 DN 98361230 PubMed ID: 9697765
 TI A functional PtdIns(3)P-binding motif.
 CM Comment in: Nature. 1998 Jul 30;394(6692):426-7
 AU Patki V; Lawe D C; Corvera S; Virbasius J V; Chawla A
 SO NATURE, (1998 Jul 30) 394 (6692) 433-4.
 Journal code: NSC; 0410462. ISSN: 0028-0836.
 CY ENGLAND: United Kingdom
 DT Letter
 LA English
 FS Priority Journals
 EM 199808

ED Entered STN: 19980820
Last Updated on STN: 19980820
Entered Medline: 19980813

L10 ANSWER 8 OF 8 MEDLINE

Full-text

AN 1998367559 MEDLINE
DN 98367559 PubMed ID: 9702203
TI Phosphatidylinositol(3)-phosphate signaling mediated by specific binding
to RING FYVE domains.
AU Burd C G; Emr S D
CS Howard Hughes Medical Institute, University of California, San Diego
School of Medicine, La Jolla 92093-0668, USA.
SO MOLECULAR CELL, (1998 Jul) 2 (1) 157-62.
Journal code: C5E; 9802571. ISSN: 1097-2765.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980910
Last Updated on STN: 19980910
Entered Medline: 19980831
AB Phosphoinositide 3-kinases (PI(3)K) are important regulators of receptor
signaling cascades and intracellular membrane trafficking. To date, no
protein domain has been identified that binds specifically to Ptdlns(3)P
and thereby recruits/activates downstream effectors of Ptdlns(3)P
signaling. Using an in vivo assay in yeast that detects Vps34
PI(3)K-dependent intracellular localization of a GFP reporter protein, and
in vitro lipid-binding assays, we demonstrate that cysteine-rich RING
domains of the FYVE finger subfamily bind specifically to Ptdlns
phosphorylated exclusively at the D-3 position of the inositol ring.
GFP-FYVE domain fusion proteins localized predominantly to membranes of
endocytic compartments and required active Vps34 PI(3)K. Our data
establish a molecular link between Vps34 PI(3)K and several FYVE
domain-containing proteins (Vac1p, Vps27p) required for vacuolar/lysosomal
protein trafficking.

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